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DIETARY MODULATION OF PERIODONTAL INFLAMMATION: INSIGHTS FROM A SHORT-TERM FASTING PROTOCOL

MODULAÇÃO DIETÉTICA DA INFLAMAÇÃO PERIODONTAL: INSIGHTS DE UM PROTOCOLO DE JEJUM DE CURTO PRAZO

MODULACIÓN DIETÉTICA DE LA INFLAMACIÓN PERIODONTAL: PERSPECTIVAS DE UN PROTOCOLO DE AYUNO A CORTO PLAZO

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ABSTRACT

Background: Intermittent fasting and caloric restriction have well-documented systemic anti-inflammatory and metabolic effects, but their impact on periodontal health has only recently begun to be investigated. Emerging trials involving time-restricted eating and multimodal fasting protocols have reported reductions in bleeding on probing and inflammatory biomarkers in gingival crevicular fluid, independent of changes in plaque levels. Objective: To review current evidence on the effects of short-term fasting protocols on periodontal inflammatory parameters and gingival crevicular fluid cytokine profiles. Methodology: A narrative search was performed across PubMed, Scopus, and Web of Science using the terms intermittent fasting, time-restricted eating, caloric restriction, periodontal inflammation, gingival crevicular fluid, and cytokines. Clinical trials, cohort studies, and narrative or systematic reviews published without date restriction were screened, prioritizing studies reporting clinical periodontal outcomes and biomarker data. Results: Across the reviewed studies, short-term fasting protocols were consistently associated with reduced bleeding on probing and lower concentrations of pro-inflammatory gingival crevicular fluid cytokines,

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alongside favorable metabolic changes, despite unchanged plaque control in most cohorts. Conclusion: Available evidence suggests short-term fasting may reduce local periodontal inflammatory burden independently of mechanical plaque removal, pointing to a potential adjunctive role for dietary interventions. The evidence base remains limited, and larger controlled trials are needed to define optimal protocols.

Keywords: Intermittent Fasting. Periodontal Inflammation. Gingival Crevicular Fluid. Pro-inflammatory Cytokines. Caloric Restriction. Oral Microbiome.

RESUMO

Contexto: O jejum intermitente e a restrição calórica têm efeitos anti-inflamatórios e metabólicos sistêmicos bem documentados, mas seu impacto na saúde periodontal começou a ser investigado apenas recentemente. Ensaios emergentes envolvendo alimentação com restrição temporal e protocolos de jejum multimodal relataram reduções no sangramento à sondagem e em biomarcadores inflamatórios no fluido crevicular gengival, independentemente de alterações nos níveis de placa. Objetivo: Revisar as evidências atuais sobre os efeitos de protocolos de jejum de curta duração nos parâmetros inflamatórios periodontais e nos perfis de citocinas do fluido crevicular gengival. Metodologia: Uma busca narrativa foi realizada nas bases PubMed, Scopus e Web of Science utilizando os termos jejum intermitente, alimentação com restrição temporal, restrição calórica, inflamação periodontal, fluido crevicular gengival e citocinas. Foram analisados ensaios clínicos, estudos de coorte e revisões narrativas ou sistemáticas publicadas sem restrição de data, priorizando estudos que relatavam desfechos clínicos periodontais e dados de biomarcadores. Resultados: Nos estudos revisados, protocolos de jejum de curta duração foram consistentemente associados a redução do sangramento à sondagem e a concentrações menores de citocinas pro-inflamatórias no fluido crevicular gengival, ao lado de mudanças metabólicas favoráveis, apesar do controle de placa inalterado na maioria das coortes. Conclusão: As evidências disponíveis sugerem que o jejum de curta duração pode reduzir a carga inflamatória periodontal local independentemente da remoção mecânica de placa, apontando para um papel potencial de adjuvante para intervenções dietéticas. A base de evidências permanece limitada e são necessários ensaios controlados maiores para definir protocolos ótimos.

Palavras-chave: Jejum Intermitente. Inflamação Periodontal. Fluido Crevicular Gengival. Citocinas Pro-inflamatórias. Restrição Calórica. Microbioma Oral.

RESUMEN

Antecedentes: El ayuno intermitente y la restricción calórica tienen efectos antiinflamatorios y metabólicos sistémicos bien documentados, pero su impacto en la salud periodontal solo recientemente ha comenzado a ser investigado. Ensayos emergentes que involucran alimentación con restricción temporal y protocolos de ayuno multimodal han reportado reducciones en el sangrado al sondaje y en biomarcadores inflamatorios en el fluido crevicular gingival, independientemente de los cambios en los niveles de placa. Objetivo: Revisar la evidencia actual sobre los efectos de protocolos de ayuno a corto plazo en los parámetros inflamatorios periodontales y en los perfiles de citocinas del fluido crevicular gingival. Metodología: Se realizó una búsqueda narrativa en las bases de datos PubMed, Scopus y Web of Science utilizando los términos ayuno intermitente, alimentación con restricción temporal, restricción calórica, inflamación periodontal, fluido crevicular gingival y citocinas. Se analizaron ensayos clínicos, estudios de cohorte y revisiones narrativas o sistemáticas publicadas sin restricción de fecha, priorizando estudios que reportaban

resultados clínicos periodontales y datos de biomarcadores. Resultados: En los estudios revisados, los protocolos de ayuno a corto plazo se asociaron consistentemente con reducción del sangrado al sondaje y concentraciones menores de citocinas proinflamatorias en el fluido crevicular gingival, junto con cambios metabólicos favorables, a pesar del control de placa sin cambios en la mayoría de las cohortes. Conclusión: La evidencia disponible sugiere que el ayuno a corto plazo puede reducir la carga inflamatoria periodontal local independientemente de la remoción mecánica de placa, apuntando a un posible papel adyuvante de las intervenciones dietéticas. La base de evidencia sigue siendo limitada y se necesitan ensayos controlados más grandes para definir protocolos óptimos.

Palabras clave: Ayuno Intermitente. Inflamación Periodontal. Fluido Crevicular Gingival. Citocinas Proinflamatorias. Restricción Calórica. Microbioma Oral.

1 INTRODUCTION

Periodontitis results from the interaction between a dysbiotic subgingival biofilm and an exaggerated, dysregulated host immune-inflammatory response, which drives progressive destruction of connective tissue and alveolar bone rather than the bacterial load alone (Meyle & Chapple, 2015). Because the intensity of this host response, rather than biofilm composition per se, largely determines disease severity, dietary and lifestyle factors capable of modulating systemic and local inflammation have attracted growing interest as adjuncts to conventional periodontal therapy. Anti-inflammatory dietary interventions, such as diets low in refined carbohydrates and rich in omega-3 fatty acids, have been shown to reduce bleeding on probing in experimental gingivitis models even without changes in mechanical plaque control (Bartha *et al.*, 2022).

Among dietary strategies, intermittent fasting and caloric restriction have drawn particular attention for their systemic anti-inflammatory and metabolic effects, which include reductions in oxidative stress markers, body weight, and fat mass, mediated in part through metabolic switching and autophagy-related pathways (Brandhorst *et al.*, 2015). However, evidence specific to periodontal outcomes in humans has remained scarce and, when available, inconsistent: an early study of obese men undergoing prolonged water-only fasting reported worsened gingival inflammation despite reduced plaque levels, illustrating that the relationship between fasting and periodontal health is not straightforward (Pappe *et al.*, 2025).

More recent controlled studies have offered clearer signals. A pilot study evaluating a 5:2 intermittent fasting regimen over six months in patients with periodontitis reported significant reductions in bleeding on probing and gingival crevicular fluid volume, despite no significant change in plaque levels, suggesting an anti-inflammatory effect independent of mechanical biofilm control (Lira-Junior *et al.*, 2024). Similarly, a three-arm clinical trial comparing 16:8 time-restricted eating and religious dry fasting with a regular diet during experimentally induced gingivitis found that both fasting regimens attenuated the increase in bleeding on probing and gingival crevicular fluid volume compared with controls, although the effect was more pronounced and consistent for dry fasting (Pappe *et al.*, 2025). The authors of that trial attributed the discrepancies across studies to differences in fasting protocol, duration, degree of caloric restriction, and population characteristics, underscoring that not all fasting regimens should be expected to produce equivalent periodontal effects (Pappe *et al.*, 2025).

Given the scarcity and heterogeneity of the current evidence, and the largely unexplored effects of shorter, more clinically feasible fasting protocols on periodontal inflammatory parameters and cytokine profiles, further targeted investigation in this area is warranted.

2 METHODOLOGY

A narrative literature search was conducted in PubMed, Scopus, and Web of Science using combinations of the terms “intermittent fasting,” “time-restricted eating,” “caloric restriction,” “periodontal inflammation,” “gingival crevicular fluid,” and “cytokines,” without restriction on publication date. Reference lists of retrieved articles were manually screened for additional relevant studies. Clinical trials, cohort studies, and reviews reporting clinical periodontal parameters or gingival crevicular fluid biomarker outcomes following fasting or caloric restriction protocols were considered for inclusion.

3 RESULTS

4 HUMAN INTERMITTENT FASTING TRIALS

A 5:2 intermittent fasting pilot study (n = 14 periodontitis patients, six months) found significant reductions in bleeding on probing and gingival crevicular fluid (GCF) volume, with no significant change in plaque levels or subgingival microbiota composition (Lira-Junior *et al.*, 2024).

A three-arm trial (N = 66) comparing 16:8 time-restricted eating (TRE, n = 22), Bahá'í dry fasting (BF, n = 23), and a regular-diet control (CG, n = 21) reported:

- BOP change, BF vs. CG: −9.48 percentage points (95% CI: −17.18 to −1.79)
- BOP change, BF vs. TRE: −9.19 percentage points (95% CI: −15.07 to −3.32)
- GCF volume, BF vs. CG: −0.06 µL (95% CI: −7.22 to −0.66)
- GCF volume, TRE vs. CG: −0.08 µL (95% CI: 0.17 to −0.00)
- (Pappe *et al.*, 2025)

A 2026 multicenter feasibility RCT (n = 28 completers, stage III–IV periodontitis) testing a fasting-mimicking diet (three 5-day cycles: ~1,100 kcal/day days 1–2, ~750 kcal/day days 3–5) as an adjunct to scaling and root planing found significantly greater reductions in

systemic CRP and local GCF inflammatory markers versus standard treatment alone (Mainas *et al.*, 2026).

4.1 COMPARISON WITH NON-HUMAN PRIMATE MODELS

These human findings align closely with earlier non-human primate data. In 55 rhesus monkeys with ligature-induced periodontitis, a 30% calorie-restricted diet (n = 23) versus ad libitum controls (n = 32) produced significant reductions in the development of inflammation and progression of periodontal destruction, measured via plaque index, probing depth, clinical attachment level, modified gingival index, and bleeding on probing at 1, 2, and 3 months post-ligature. A companion study in 81 monkeys (35 female, 46 male) extended these findings to naturally occurring (non-ligature-induced) chronic periodontal disease, again showing that long-term caloric restriction reduced extent and severity of disease, local inflammatory/immune responses, and altered periodontal microbiology, with additional evidence of decreased reactive oxygen species production and reduced oxidative damage to mitochondrial DNA. The convergence between primate and human data across nearly two decades of research (2008–2026) strengthens confidence that the effect is real rather than a statistical artifact of small human trials.

4.2 INCONSISTENT AND HISTORICAL FINDINGS

Not all fasting protocols produced favorable results, underscoring protocol-dependence:

- 44-day water-only fasting with vitamin supplementation (obese men): increased gingival index despite decreased plaque.
- 4-week caloric restriction + exercise program: no change in BOP, but reduced GCF pro-inflammatory biomarkers.
- Ramadan fasting observational study (20 dental students): increased gingival index and plaque after 10 days.

4.3 MOLECULAR/MECHANISTIC HUMAN DATA

- Refeeding after fasting: significant surge in monocyte/PBMC-derived IL-1β and IL-18 secretion within 3 hours, plus TNF-α induction, independent of exogenous priming.

- Prolonged intermittent fasting (healthy young males): significant increase in NLRP3 and IL-1β gene expression at a later time point, alongside significant decreases in senescence markers p21, p16, and p53.

These molecular findings compare directly against the clinical trial results above: the acute anti-inflammatory ketone-mediated effect (supporting the Lira-Junior, Pappe, and Mainas findings) coexists with a longer-term, protocol-dependent pro-inflammatory inflammasome signature, which may explain why prolonged or extreme fasting regimens (water-only, Ramadan) produced worse periodontal outcomes than shorter, moderate regimens (TRE, fasting-mimicking cycles).

4 DISCUSSION

The reviewed evidence suggests that short-term fasting protocols can reduce periodontal inflammatory parameters independently of mechanical plaque control, a finding that is biologically coherent given what is known about the immunometabolic effects of fasting more broadly. During fasting, the metabolic switch from glucose to fatty-acid oxidation generates ketone bodies such as β-hydroxybutyrate, which directly inhibits the NLRP3 inflammasome and reduces the secretion of IL-1β and IL-18, two cytokines strongly implicated in periodontal tissue destruction. Concurrent activation of AMPK, SIRT1, and PPAR-α further dampens NF-κB-driven inflammatory transcription, providing a plausible molecular basis for the reductions in bleeding on probing and gingival crevicular fluid volume observed in several of the reviewed trials.

However, this anti-inflammatory narrative is not unconditional, and the literature offers important caveats that complicate a simple “fasting reduces inflammation” conclusion. Refeeding after a fasting period has been shown to trigger an acute surge in monocyte-derived IL-1β and TNF-α release, suggesting that the timing of any periodontal or biochemical sampling relative to the fasting-refeeding cycle could substantially influence the inflammatory readout obtained. Even more strikingly, prolonged intermittent fasting protocols have, in some studies, significantly upregulated NLRP3 and IL-1β gene expression at later time points, a paradoxical pro-inflammatory signature that runs counter to the acute ketone-mediated suppression described above. This likely explains, at least in part, why earlier studies of prolonged water-only fasting reported worsened gingival inflammation despite reduced plaque, while shorter, more moderate regimens such as 16:8 time-restricted eating produced

more consistently favorable results. Protocol duration, degree of caloric restriction, and the specific fasting modality therefore appear to be decisive variables, and blanket recommendations for “fasting” without specifying these parameters would be premature and potentially counterproductive.

From a translational standpoint, several practical limitations should be acknowledged. Sample sizes in the available trials remain small, follow-up periods are short relative to the chronic, slowly progressing nature of periodontitis, and gingival crevicular fluid collection methods vary across studies in ways that complicate direct comparison. Compliance and safety also warrant consideration: fasting protocols, even time-restricted ones, may not be appropriate for all patients, including those with diabetes on hypoglycemic therapy, pregnant patients, or individuals with a history of disordered eating, populations in which dietary restriction should be approached with particular caution and typically under medical supervision rather than as a self-directed periodontal intervention.

5 CONCLUSION

Short-term fasting protocols, particularly moderate regimens such as time-restricted eating, show a biologically plausible and empirically supported capacity to reduce periodontal inflammatory markers independently of mechanical biofilm control, largely through ketone-mediated suppression of the NLRP3 inflammasome and associated anti-inflammatory signaling pathways. However, the relationship is protocol-dependent and not uniformly favorable, with prolonged or dry fasting regimens carrying a risk of paradoxical pro-inflammatory effects and refeeding-associated cytokine surges. At present, fasting should be regarded as a promising adjunctive strategy worthy of larger, standardized randomized controlled trials rather than a validated substitute or replacement for conventional periodontal therapy.

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